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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,296	03/21/2001	Laura L. Kiessling	1-00	4642

23713 7590 06/03/2004

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EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/815,296	KIESSLING ET AL.	
	Examiner	Art Unit	
	Mark Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-157* is/are pending in the application.

4a) Of the above claim(s) *4-16, 24-27, 31-40, 43-58, 61, 63, 65, 67, 69, 70, 75-80, 87-89, 93, 96-139 and 156* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *147* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/10/02&11/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 1-3,17-23,28-30,41,42,59,60,62,64,66,68,71-74,81-86,90-92,94,95,140-146,148-155 and 157.

DETAILED ACTION

Claims

Currently, claims 1-157 are pending. Claims 1-3, 17-23, 28-30, 41, 42, 59, 60, 62, 64, 66, 68, 71-74, 81-86, 90-92, 94, 95, 140-146, and 148-155 and 157 are examined. Claims 4-16, 24-27, 31-40, 43-58, 61, 63, 65, 67, 69, 70, 75-80, 87-89, 93, 96-139 and 156 are withdrawn from consideration as non-elected. Claim 147 is objected to and has been withdrawn from consideration.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1 [in part], claims 2-47, 56-95 and 140-141) and the election of species of human cells, release of intracellular signal, ROMP-formylated peptide having the structures as set forth in the Response at pp. 27-28 in the Response, filed 3/4/2004, to the previous Requirement for Restriction/Election, mailed 9/4/2003, is acknowledged.

Applicant traverses the restriction requirement on the ground(s) that the examiner has not stated what different steps or reagents differentiate the *in vitro* and *in vivo* methods; that the differences in steps, reagents and results between Group I and Group II would not represent an undue burden that requires restriction. Applicant argues the there ability to write a claim that encompasses *in vivo*, *in vitro*, and *ex vivo*, demonstrates a significant overlap in cell type, overlap in biological process and overlap in type of multivalent ligand. Applicant argues that the difference between *in vivo* and *in*

vitro methods at most amounts to another requirement of election of species because applicant is entitled to examination of a reasonable number of distinct species that are linked by allowable generic claims. Applicant traverses the election of species "because the application contains allowable generic claims (such as claim 1, claim 28 and claim 144] which are allowable."

This is not found persuasive because the steps, reagents, and results for *in vivo* methods are different from *in vitro* methods, would require, for example, the step of administering to a living animal, living animal substrates, and whole animal assay results, and therefore have different issues regarding patentability and enablement and represent patentably distinct subject matter that would place an undue search burden on examination. Applicant's argument that there is significant overlap in cell type, overlap in biological process and overlap in type of multivalent ligand does not address the critical differences of whole animal experimentation, which is much more complex than an *in vitro* assay system, and involves many biological systems, including circulatory, renal, intestinal and hepatic organ systems. Therefore, the *in vitro* invention of the claimed invention is separate and distinct from *ex vivo* and *in vivo* inventions. Because claim 156 is drawn to *in vitro* or *ex vivo* methods, it has been withdrawn as drawn to a non-elected invention.

Applicant's traversal of the requirement for election of species on the ground that the generic claims are allowable does not distinctly and specifically point out the supposed errors in the restriction requirement, and is not persuasive.

Applicant, in the Response, filed 3/4/2004, to the previous Requirement for Restriction/Election mailed 9/4/2003, elected the species of release of an intracellular signal (B4, from list on page 8 of the Requirement for Restriction/Election, mailed 9/4/2003). However, claims 24-27 are drawn to chemotaxis, which is a different listed species from that of release of an intracellular signal. Claims 24-27 have therefore been withdrawn as drawn to a non-elected species.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement filed 10/10/2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. No copies have been received.

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing

application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). The amendment to the specification, filed 3/04/2004, regarding reference 67, of Ranaschi et al., is improper because the amendment was not accompanied by an affidavit or declaration.

Claim Objections

Claim 81 is objected to because claim 81 recites the term "ROMP", which is an abbreviation. The claim must provide this words for which this term stands.

Claim 147 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 147 is recites: "The method of claim 142 wherein **n** is 50 or more." However, neither any of claim 142, or claims 17, 2 or 1, from which claim 142 depends, recites the limitation "**n**".

Claims 156 and 157 are objected to because of the following informalities: In the amendment to the claims, filed 3/4/2004, the status of claims 156 and 157 is not provided. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 152 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

Applicant, in the remarks filed 3/4/2004, states that support for claim 152 may be found in the amendment to the specification at p. 7, based on the incorporation by reference of cited reference 67, of Ranaschi et al. However, applicant's amendment to the specification by incorporation by reference is improper. The amendment to the specification incorporating by reference the essential matter of cited reference 67 of Ramashi et al. must be accompanied by an affidavit or declaration, as stated above.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 17-23, 28-30, 41, 42, 59, 60, 62, 64, 66, 68, 71-74, 81-86, 90-92, 94, 95, 140-146, and 148-155 and 157 are rejected under 35 U.S.C. § 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and its dependent claims, recite the language "and bonded to a molecular scaffold", which renders the claims indefinite, because it is unclear as to whether it is the multivalent ligand or the signal recognition elements that is bonded to the molecular scaffold.

Claim 19 recites the language "wherein signal transduction is mediated by receptors", which renders the claim vague and indefinite, because claim 18, from which claim 19 depends, recites the language "the multivalent ligand modulates transduction mediated by G-protein coupled receptors", so that it is not clear whether the "receptors" of claim 19 are the "G-coupled receptors" of claim 18.

Claim 82, and its dependent claims, recite the language '"BB"', which renders the claims vague and indefinite, because there is no '"BB"' in the structure depicted. Also, claim 82 recites the language '"BB" represents the backbone repeating unit, which may be cyclic or acyclic, and may be the same or different in a random or block arrangement', which renders the claims vague and indefinite, because it is not clear how a backbone repeating unit, BB, may be *different* or in a *random* arrangement. The instant claim recites the terms RE and SRE, which are abbreviation; the claim must provide the words for which these terms stand.

Claim 91, and its dependent claims, recite the language '"BB"', which renders the claims vague and indefinite, because there is no '"BB"' in the structure depicted. Also, claim 82 recites the language '"BB" represents the backbone repeating unit, which may

be cyclic or acyclic, and may be the same or different in a random or block arrangement', which renders the claims vague and indefinite, because it is not clear how a backbone repeating unit, BB, may be *different* or in a *random* arrangement. The instant claim recites the terms SRE, which is an abbreviation; the claim must provide the words for which this term stands.

Claim 83-86 recite the terms SRE, which is an abbreviation; the claims must provide the words for which this term stands.

Claim 90 recites the terms RE, which is an abbreviation; the claim must provide the words for which this term stands.

Claims 91, 92, 94 and 95, recite the terms SRE, which is an abbreviation; the claims must provide the words for which this term stands.

Claim 144 recites the terms SRE, FE, and RE, which are abbreviations; the claim must provide the words for which these terms stand.

Claim 148 recites the terms SRE, FE, and RE, which are abbreviations; the claim must provide the words for which these terms stand.

Claims 149 and 150 recite the terms SRE, which is an abbreviation; the claims must provide the words for which this term stands.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 81, 82, 83, 85, 86, and 90 are rejected under 35 U.S.C. § 102(a) as being anticipated by Gordon et al., (Chemistry & Biology 2000, vol. 7:9-16).

Claims 1, 81, 82, 83, 85, 86, and 90 are drawn to methods for inducing a biological response in a biological system comprising one or more receptors wherein a multivalent ligand comprising a plurality of signal recognition elements wherein the signal recognition elements are recognized by at least one of the receptors and wherein the signal recognition elements are bonded to molecular scaffold; wherein the multivalent ligand has the general formula of claim 82, and has functional groups that act as markers.

Gordon throughout the publication and at the abstract, p. 9, para 4-p. 10, para 2, teaches, teaches using ring-opening metathesis polymerization (ROMP) to generate to form multivalent arrays that include multivalent ligands for binding to cell surface receptors, e.g. through epidermal growth factor; teaches at Figures 3-5, polymers of the general formula of claims 82 and 91, at p. 13, para 2 and 3, teaches multivalent ligands coupled to a fluorescent reporter group that is fluoresce in, where the signal recognition element binds to L-selectin, which acts to recruit white cells to sites of tissue damage,

and so acts as a guide to cells, i.e., chemoattractant, as demonstrated on human T-cells (Jurkat cells).

Claims 1-3, 17, 20-23, 28-30, 41, 42, 59, 60, 62, 64, 68, 71-74, 140, 142, 143, 151, 154, 155, 157 are rejected under 35 U.S.C. § 102(b) as being anticipated by Whitesides et al., WO 98/46270 (reference 4, IDS filed 10/10/2002).

Claims 1-3, 17, 20-23, 28-30, 41, 42, 59, 60, 62, 64, 68, 71-74, 140, 142, 143, 151, 154, 155, 157 are drawn to methods for inducing a biological response in a biological system comprising one or more receptors wherein a multivalent ligand comprising a plurality of signal recognition elements wherein the signal recognition elements are recognized by at least one of the receptors and wherein the signal recognition elements are bonded to molecular scaffold; and various biological responses thereby.

Whitesides, throughout the publication and at p. 3, lines 11-24, p. 7, lines 24-31, p. 14, lines 1-9, p. 15, lines 20-31, teaches multivalent ligands on a polymeric backbone of the form $Y-(A)_n$, where Y is a framework, A is a functional group, and n is an integer greater than 10, 50 or more, or about 100 or more and wherein the functional group that is a signal recognition is covalently bonded to the framework that is a molecular scaffold, such as a liposome; teaches at p. 32, lines 7-13, polyvalent presenters that include Sialyl Le^x that bind leukocyte receptor sites including integrins and selectins and are elements involved in signal recognition, inducing intracellular and intercellular responses; teaches at p. 60, line 26-p.61, line 20 modulation of cell-cell interactions by

polyvalent presenters, (which include multivalent ligands), whereby numerous cell-cell interactions can be promoted or inhibited, such as neutrophil attachment to endothelial cells during inflammation; teaches at Table 2, p. 62, line 4-p. 63, line 7, cell-cell interactions that include neutrophil, endothelial cells, T–cells, and the release of platelet granules; teaches at p. 87, lines 3-18, teaches cytokine production by replacing a stimulator cell in a cell-cell interaction that normally leads to cytokine secretion, e.g., the L-selectin ligands to simulate monocytes and macrophages to produce tumor necrosis factor; teaches at p. 96, line 1-p. 99 line 16, *in vitro* assays; at p. 97, line 31- p. 99, line 16, teaches cross-linking multivalent receptors on the cell by agglutinins to prevent the biological response of viral binding to the cell surface.

Claims 1, 81, 82, 83, 85, and 90 are rejected under 35 U.S.C. § 102(e) as being anticipated by Kiessling et al., US 6,291,616, (reference 1, IDS filed 10/10/2002).

Claims 1, 81, 82, 83, 85, and 90 are drawn to methods for inducing a biological response in a biological system comprising one or more receptors wherein a multivalent ligand comprising a plurality of signal recognition elements wherein the signal recognition elements are recognized by at least one of the receptors and wherein the signal recognition elements are bonded to molecular scaffold; wherein the multivalent ligand has the general formula of claim 82, and has functional groups that act as markers.

Kiessling et al., US 6,291,616, at col. 1, lines 10-48, teaches using ring-opening metathesis polymerization (ROMP) to generate to form multivalent arrays that include

multivalent ligands for binding to cell surface receptors, e.g. through epidermal growth factor, resulting in dimerization of the transmembrane receptor; teaches at col. 10, line 32-col. 11, line 46, polymers of the general formula of claims 82 and 91, col. 13, line 44-col. 14, line 32, teaches multivalent ligands coupled to a fluorescent reporter group that is fluoresce in, where the signal recognition element binds to L-selectin, which acts to recruit white cells to sites of tissue damage, and so acts as a guide to cells, i.e., chemoattractant, as demonstrated on human T-cells (Jurkat cells).

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 2, 17, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitesides et al., WO 98/46270, (reference 4, IDS filed 10/10/2002) and Shea et al., Biophysical Journal, 1997, vol. 73, pp. 2949-2959.

Claims 1, 2, 17, 18 and 19 are drawn to methods for inducing a biological response in a biological system comprising one or more receptors wherein a multivalent

ligand comprising a plurality of signal recognition elements wherein the signal recognition elements are recognized by at least one of the receptors and wherein the signal recognition elements are bonded to molecular scaffold, wherein the multivalent ligand modulates signal transduction mediated by G-protein coupled receptors.

Whitesides, throughout the publication and at p. 3, lines 11-24, p. 7, lines 24-31, p. 14, lines 1-9, p. 15, lines 20-31, teaches multivalent ligands on a polymeric backbone of the form $Y-(A)_n$, where Y is a framework, A is a functional group, and n is an integer greater than 10, 50 or more, or about 100 or more and wherein the functional group that is a signal recognition is covalently bonded to the framework that is a molecular scaffold, such as a liposome; teaches at p. 32, lines 7-13, polyvalent presenters that include Sialyl Le^x that bind leukocyte receptor sites including integrins and selectins and are elements involved in signal recognition, inducing intracellular and intercellular responses; teaches at p. 60, line 26-p.61, line 20 modulation of cell-cell interactions by polyvalent presenters, (which include multivalent ligands), whereby numerous cell-cell interactions can be promoted or inhibited, such as neutrophil attachment to endothelial cells during inflammation; teaches at Table 2, p. 62, line 4-p. 63, line 7, cell-cell interactions that include neutrophil, endothelial cells, T–cells, and the release of platelet granules; teaches at p. 87, lines 3-18, teaches cytokine production by replacing a stimulator cell in a cell-cell interaction that normally leads to cytokine secretion, e.g., the L-selectin ligands to simulate monocytes and macrophages to produce tumor necrosis factor; teaches at p. 96, line 1-p. 99 line 16, *in vitro* assays; at p. 97, line 31- p. 99, line

16, teaches cross-linking multivalent receptors on the cell by agglutinins to prevent the biological response of viral binding to the cell surface.

Whitesides et al. does not teach G protein coupled receptors.

Shea et al., teach the G-protein activation and formation of cross-linked receptors by multivalent ligands. Shea, at the abstract, and p. 2949, para 1, teaches the initiation the cascade of signal transduction by multivalent ligand binding to G-protein coupled receptors in the plasma membrane, which acts as a first step.

It would have *prima facie* obvious for one of ordinary skill in the art at the time of the invention to combine methods for inducing biological response by multivalent ligands with multivalent ligands that modulate signal transduction mediated by G-protein coupled receptors.

One of ordinary skill in the art would have been motivated to use multivalent ligands that modulate signal transduction mediated by G-protein coupled receptors, in order to initiate a biological response that is a cascade of signal transduction, as taught by Shea et al.

Claims 1, 62, 64, 66, 82, 83, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitesides et al., WO 98/46270 (reference 4, IDS filed 10/10/2002), Kiessling et al., US 6,291,616 (reference 1, IDS filed 10/10/2002), and Painter et al., Journal of Cell Biology, 1987, vol. 105, pp. 2959-2971.

Claims 1, 62, 64, 66, 82, 83, and 84 are drawn to methods for inducing a biological response in a biological system comprising one or more receptors wherein a

multivalent ligand comprising a plurality of signal recognition elements wherein the signal recognition elements are recognized by at least one of the receptors and wherein the signal recognition elements are bonded to molecular scaffold, and wherein the signal recognition element is a derivatized peptide and is an N-formylated peptide.

Whitesides, throughout the publication and at p. 3, lines 11-24, p. 7, lines 24-31, p. 14, lines 1-9, p. 15, lines 20-31, teaches multivalent ligands on a polymeric backbone of the form $Y-(A)_n$, where Y is a framework, A is a functional group, and n is an integer greater than 10, 50 or more, or about 100 or more and wherein the functional group that is a signal recognition is covalently bonded to the framework that is a molecular scaffold, such as a liposome; teaches at p. 32, lines 7-13, polyvalent presenters that include Sialyl Le^x that bind leukocyte receptor sites including integrins and selectins and are elements involved in signal recognition, inducing intracellular and intercellular responses; teaches at p. 60, line 26-p.61, line 20 modulation of cell-cell interactions by polyvalent presenters, (which include multivalent ligands), whereby numerous cell-cell interactions can be promoted or inhibited, such as neutrophil attachment to endothelial cells during inflammation; teaches at Table 2, p. 62, line 4-p. 63, line 7, cell-cell interactions that include neutrophil, endothelial cells, T–cells, and the release of platelet granules; teaches at p. 87, lines 3-18, teaches cytokine production by replacing a stimulator cell in a cell-cell interaction that normally leads to cytokine secretion, e.g., the L-selectin ligands to simulate monocytes and macrophages to produce tumor necrosis factor; teaches at p. 96, line 1-p. 99 line 16, *in vitro* assays; at p. 97, line 31- p. 99, line

16, teaches cross-linking multivalent receptors on the cell by agglutinins to prevent the biological response of viral binding to the cell surface.

Kiessling et al., US 6,291,616, at col. 1, lines 10-48, teaches using ring-opening metathesis polymerization (ROMP) to generate to form multivalent arrays that include multivalent ligands for binding to cell surface receptors, e.g. through epidermal growth factor, resulting in dimerization of the transmembrane receptor; teaches at col. 10, line 32-col. 11, line 46, polymers of the general formula of claims 82 and 91, col. 13, line 44-col. 14, line 32, teaches multivalent ligands coupled to a fluorescent reporter group that is fluoresce in, where the signal recognition element binds to L-selectin, which acts to recruit white cells to sites of tissue damage, and so acts as a guide to cells, i.e., chemoattractant, as demonstrated on human T-cells (Jurkat cells).

Neither of Whitesides et al. or Kiessling et al. do teach a derivatized peptide that is an N-formylated peptide, US 6,291,616, teach methods for inducing a biological response by multivalent ligands, wherein the signal recognition element is a derivatized peptide and is an N-formylated peptide.

Painter et al. teach a derivatized peptide that is an N-formylated peptide that is a ligand that binds to a glycoprotein receptor and acts as a recognition element to stimulate chemotaxis of human neutrophils.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to combine methods of inducing biological response by multivalent ligands that bind to receptors, with derivatized or N-formylated peptides.

One of ordinary skill in the art would have been motivated to use derivatized or N-formylated peptides in multivalent ligands in order to stimulate chemotaxis of human neutrophils, as taught by Painter et al.

Conclusion

Claims 1-3, 17-23, 28-30, 41, 42, 59, 60, 62, 64, 66, 68, 71-74, 81-86, 90-92, 94, 95, 140-146, and 148-155 and 157 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Shibuya
Examiner
Art Unit 1639

ms

ADMASHRI PONNALURI
PRIMARY EXAMINER